Spring 2007
Industry Study

Final Report
Biotechnology Industry

The Industrial College of the Armed Forces
National Defense University
Fort McNair, Washington, D.C. 20319-5062

BIOTECHNOLOGY 2007

ABSTRACT

Biotechnology is a diverse and promising industry, but it is not without challenges. The impact on our lives is already being felt, and all indications point to a future of unprecedented changes. Genetically modified (GM) organisms are being used to increase crop production, bacteria to remediate contaminated areas, and even fetal calf skin to grow human soft tissues. Concurrently our nation is seeking biotechnology answers for a variety of national security issues, including the defense of biological or chemical attack and pandemic influenzas. Biotechnology is rapidly impacting multiple industries including medicine, defense, energy, and agriculture. This paper addresses four general biotechnology areas: medical, emerging technology, biodefense, and agriculture. These discussions range from personalized medicine, pandemics and vaccines to biofuels and Project BiosShield. The potential economic impact of the industry is tremendous and leads directly to many of the challenges our nation will face in the future. These challenges include globalization, government regulation, ethical concerns and societal acceptance. As the biotechnology industry continues to mature, we expect to see a bright future where the benefits of biotechnology will outweigh the risks involved in its application.

COL Kyle D. Campbell, USA
COL Gene Clemen, Philippine Marine Corps
Mr. Paul Denham, IBM
Col Greg Dodson, USAF
Ms. Denise Flanagan, DN
COL Dale Goble, USA
Lt Col Deirdre Mahon, USAF
Ms. Joanne Martin, State
CDR Rick Merrill, USN
COL Mike Milford, Australian Army
LtCol Bruce Nickle, USMC
Mr. Jim Omans, DN
Mr. Ramu Pillai, DCMA
CAPT Steve Schmeiser, USN
Col John Stutts, USAF

Dr. Joseph E. Goldberg, Faculty
COL John Sees, Faculty
COL Paul T. Bartone, Faculty

PLACES VISITED

Domestic

Armed Forces Institute of Pathology Laboratory, Rockville, MD
Walter Reed Army Institute of Research, Silver Spring, MD
MedImmune, Gaithersburg, MD
Human Genome Sciences, Rockville, MD
Merial Limited, Duluth, GA
Centers for Disease Control and Prevention, Athens, GA
U. S. Department of Agriculture, Agricultural Research Center, Beltsville, MD
United States Army Medical Research Institute of Infectious Diseases, Ft. Detrick, MD
Charles River Laboratories, Wilmington, MA
Harvard Stem Cell Institute, Boston, MA
TEI Biosciences, Boston, MA
Genzyme, Cambridge, MA
Broad Institute, Cambridge, MA
GTC Biotherapeutics, Framingham, MA

International

Center for Biotechnology, Jawaharlal Nehru University, New Delhi, India
International Center for Genetic Engineering and Biotechnology, New Delhi, India
U.S. Embassy, New Delhi, India
Government of India Department of Biotechnology, New Delhi, India
Indian Institute of Technology, Department of Biotechnology, New Delhi, India
Ranbaxy Laboratories Limited, Gurgaon, India
Indian Defence Research and Development Organisation, Ministry of Defense, New Delhi, India
Reliance Inc., Dhirubhai Ambani Reliance Life Sciences Centre, Mumbai, India

INTRODUCTION AND INDUSTRY DEFINITION

Biotechnology touches nearly every aspect of our daily lives from the clothing we wear, the fuel we use, the food we eat, and the medicines we take. From the earliest days, humans have used the principles of biotechnology to improve their daily lives by fermenting fruit, making bread using yeast, and making yogurt from milk. Biotechnology has evolved from a process driven science of simply manipulating organisms to a technique driven science of combining cells and molecules with other forms of science and technologies (Grace, 2006, p. 2). The current rise of biotechnology stems from the ability to fuse various sciences and specialties, such as life sciences, chemistry, industrial engineering, computational science, and physics with biology.

Biotechnology itself "is an umbrella term that covers various techniques for using the properties of living things to make products or services" (Grace, 2006, p. 2). The US biotechnology industry is very broad and includes health care, food, agriculture, industrial, and environmental industries. It is one of the fastest growing sciences and industries in the US and is facilitating expansion and development in an unprecedented number of areas. Specifically, biotechnology manipulates cells and molecules to bioengineer living organisms to make resources or commercial products (medicines, seeds, fuel).

In addition, modern biotechnology has provided an understanding of the human genome, which has facilitated comprehension of the genetic makeup laying the foundation for personalized medicine which will allow physicians to better administer the proper medications and develop strategies for disease prevention. Advances in recombinant DNA sequencing will hopefully counter the threat of either a naturally or deliberately introduced pandemic. Biotechnology is also an essential element in the development of vaccines, which are the cornerstone of national preparedness against pandemics or bio-terrorist attacks. The use of GM crops provides significant health, economic, and environmental benefits and is poised to meet the demands of a growing world population and its demand for renewable resources. The emergence of biofuels as an alternative fuel source is rapidly expanding the alternative energy field to reduce the world's dependency on traditional fuels. The newest promise in biotechnology lies in nanotechnology which, among multiple capabilities, enables creation of biomolecular and molecular modeling utilized in artificial organ development. In addition to the US biotech industry, other countries offer potential for development in the field and are increasing their investment. Challenges exist, as with any industry, but the potential benefits of the biotechnology field far outweigh its possible shortcomings. The diversity, broad applications and continued development of the US biotechnology industry are critical to ensure the US can meet the many national security challenges in the 21st Century.

APPLICATIONS OF BIOTECHNOLOGY

The applications of biotechnology are many and varied and found throughout the global market place. We address nine specific areas under four related groupings including Medical, Emerging Applications, Biodefense and Agricultural. These nine areas include personalized medicine, pandemics, vaccines, bionanotechnology, bioshield, biodefense, agricultural, biofuels and cloning.

MEDICAL

Personalized medicine

Personalized medicine is a new capability resulting from scientific advances in biotechnology. Personalized medicine "refers to using information about a person's genetic makeup to tailor strategies for the detection, treatment, or prevention of disease" (Collins, 2007, p. 1). These approaches have their roots in the discovery of the structure of deoxyribonucleic acid (DNA) and the subsequent study of the human genome. DNA contains the instructions and blueprints to make every cell, of every type, in the human body. The genes are the specific DNA segments that carry the genetic information or blueprints. While this sounds clear and easy, the magnitude is overwhelming. As Dr. Francis S. Collins, Director, National Human Genome Research Institute (2007) stated, "there are 3 billion letters in the human DNA code. Yet, this 'instruction book' is 99.9 percent identical between any two humans" (p. 1). Despite this commonality, diseases and medications affect people differently. Thus, the key to more effective medical treatment appears to lie in the 0.1 percent difference. Identifying these genes and their specific actions is the core of personalized medicine.

Through the study of these genes and their actions, physicians and scientists will be able to provide beneficial drugs, optimal dosages, and reduce adverse reactions. Today, physicians do the very best they can in selecting the appropriate drug and dosage level for each particular patient. However, the system is a best guess process of trial and error. "Each year, some 100,000 Americans die from adverse reactions to medications, and more than 2 million are hospitalized. But until the dawn of pharmacogenomics, there was no way to predict how a certain individual would react to a drug. Pharmacogenomics may be able to predict who is likely to have a bad reaction to a drug before they take it. It may also be possible to predict if patients will respond well to medication" (Mayo On-line, 2006, p. 2).

In addition to better accuracy in prescribing and dosing drugs, personalized medicine has great potential in reducing the time to market for drugs while increasing safety. By pre-selecting the test population and performing the testing on fewer subjects, drug companies will lower costs with more clearly defined results from the genetically stratified populations. "Using pharmacogenomics in clinical-trial design is expected to reduce the clinical development time from 10-12 years in traditional commercialization to just 3-5 years" (PriceWaterHouseCoopers, 2007, p. 14). However, while reduced timelines indicate a potential for reduced costs, thus far the price of medications produced via personalized medicine appear to be significantly higher. In addition, given that diseases appear to result from multiple genes and proteins, and to have idiosyncratic effects on people, the continuing development of personalized medicine is sure to be challenging and complex.

Given the financial incentives and the tenacity of the world's scientific community, the practice of personalized medicine demonstrates tremendous potential. In fact, personalized medicine remains one of the most compelling opportunities to improve the odds of staying healthy. By 2010, it is likely that predictive genetic tests will be available for a dozen common conditions. This will enable individuals to take preventive steps to reduce their risks of developing various disorders. Doctors will tailor and prescribe treatments for each patient's unique genetic profile choosing medicines that are most likely to produce positive results. This information can be used to guide prescribing patterns to develop a lifelong plan of health maintenance customized to unique genetic profiles (Collins, 2007, p. 3). Personalized medicine

with all its opportunities is coming and will, one day, be as commonly accepted as blood tests are today.

Pandemics

For centuries pandemics, or global outbreaks of infectious diseases with no known human antibodies have been responsible for a great number of deaths. A pandemic is a global epidemic. Three influenza pandemics have been recorded in the last century alone. The Spanish Flu pandemic of 1918 was the most severe and claimed the lives of 50 to 100 million people. Today, a pandemic on the scale of the Spanish Flu has potential to kill 180 to 360 million people (Osterholm, 2005, ¶ 1). Because pandemics can be introduced either naturally or deliberately into the population, it is important to understand the natural mutation of viruses as compared to the deliberate use of pathogens as a weapon. Additionally, nations must have a plan to prepare for and respond to pandemics.

Unfortunately, there is a promise of inevitability when we speak about the mutation of viruses. Viruses are living creatures that seek hosts for survival and mutate continuously in order to survive; however, it is not inevitable that the mutation of viruses will lead to pandemic outbreaks. Medical technology and increased surveillance provide the capability to identify wide-scale person-to-person transmission of the H5N1 Avian Influenza subtype. Since all influenza is avian in origin, most of its variations do not present a threat to humans (Thomas, 2006, p. 921). Viruses pose the danger of pandemic when they mutate across species (zoomatic) and when the host has no antibodies. Presently, H5N1 (avian influenza) poses this threat. Such a virus could be catastrophic. Is there another lethal subtype out there waiting to attack by jumping species? Only time will tell.

According to the World Health Organization (WHO), the hallmarks of an influenza pandemic are: 1) the emergence of a novel influenza virus strain; 2) the finding that the strain can cause human disease; 3) an sustained person-to-person transmission of that strain (CRS, 2007, p. 5). Despite the human body's natural defense mechanisms, the influenza virus is an agile foe that constantly mutates. This vulnerability illustrates the need for annual vaccinations to protect against it (Bartlett, 2005, p. 460). However, annual vaccinations coupled with the flu virus' ability to mutate create a conundrum, where it could mutate creating a new virus. This mixing process is referred to as "virus sex" (Rosenwald, 2006, p. 40). A nightmare scenario would be the simultaneous infection of a mammal by both the human influenza virus and the avian influenza virus, H5N1. If the H5N1 virus mutates with a human virus allowing it to spread from human to human, we would have an influenza strain for which no human would have immunity.

Because mammals are vulnerable to infection by H5N1 from chickens as well as from human flu strains, the potential for the virus to jump species increases dramatically. The working hypothesis is that wild aquatic birds are the primordial reservoir of all influenza viruses for avian and mammalian species. Only through large-scale genetic sequencing of human influenza will the dynamic nature of viral genome evolution be revealed and additional large-scale genetic testing explain how these strains cross the species barrier and move into the human population (Ghedin, 2005, p.1165).

We have only begun to unlock the mystery of influenza virus mutation and its natural occurrence. To introduce genetically modified influenza strains to render virulent strains harmless is an achievable goal. The consequences of not pursuing this goal are catastrophic.

Anticipating virus mutation from year to year, and whether or not if the mutation will result in a strain allowing it to move from people to people efficiently is impossible. In either case, the time to isolate and identify the virulent strain and develop an effective vaccination can take months. As a result, practical measures must be implemented to prevent the mixing of genetic material resulting in potentially virulent strains of influenza. Sanitary handling of domestic poultry, waterfowl vaccination, and the segregation of species is only a start to prevent pandemic influenza.

Just as naturally introduced pandemics have been present for centuries, the use of pathogens as a weapon is not new. The use of germs or pathogens as a weapon dates back centuries. For example, during the French and Indian Wars the British distributed blankets previously used by smallpox patients (Henderson, 1999, p.2). Unfortunately, the virulent agents of past pandemics have not been completely eradicated and are still potential threats today. Age-old nemeses such as smallpox may not be footnotes in history.

The most dangerous agents, based on the greatest potential for harm to the public and the numbers of estimated casualties are: smallpox, anthrax, plague, botulism and tularemia (Rotz, 2002 p.2). The Johns Hopkins Center for Civilian Biodefense Studies stated that these diseases are potential pandemic diseases because they are communicable agents, highly transportable and lack readily available treatments and vaccines. Of these, the most dangerous are the smallpox and anthrax viruses (Hopkins Center of Civilian Biodefense Studies Symposium, 2007, p.6).

Although the threat of biological weapons is real, the probability of an attack may not be as high as with other weapons of terror. There are many reasons why the introduction of biological weapons is limited, but first and foremost is that developing an effective biological weapon is not easily done. The material is difficult to acquire as are the skills and expertise required to produce, weaponize, and deliver the pathogen to the desired target (Parachini, 2001, p.11). Despite these limitations, some countries have successfully produced pathogens. According to a former deputy director of the Soviet Union's civilian bioweapons program, the Soviet government was able to produce the smallpox virus in large quantities, along with plague, anthrax and botulinum toxin (Henderson, 1999, p. 2). Another defector claimed the former regime produced the smallpox virus by the ton (Korterpeter, 1999, p. 525). Concerns also remain about South Africa's former weapons program, which was active between 1981 and 1993. South African scientists collected hundreds of strains of deadly pathogens as part of the program, and there is no conclusive evidence that these agents were destroyed (Tucker, 2003, p. 24).

The availability of open source literature increases the potential for terrorists' misuse of biotechnology. According to Mr. Richard Guthrie, a former researcher at The Stockholm International Peace Research Institute, "the free access to genetic sequence data for human genome and a large number of other genomes, including pathogenic micro-organisms, is a great scientific resource, but it could pose a significant threat if misused" (Purkitt, 2005, p. 15). The consequences of a pandemic are too severe to dismiss as a possible weapon of choice by terrorists. Unfortunately, what can be used for human benefit can be used for harm.

While no one knows when the next pandemic will emerge or whether it will be naturally or deliberately introduced, it's imperative that our nation be prepared to respond. The document that outlines the US strategy for pandemics is the November 2005 *National Strategy for Pandemic Influenza (NSPI)*. The *NSPI* objectives are to stop, slow or limit the spread of a pandemic to the US; improve our ability to quickly produce new vaccines and stockpile vaccines and antivirals to mitigate disease, suffering, and death; and ensure America is ready to respond at the federal, state, and local levels to sustain infrastructure and maintain a functioning economy

and society. To meet these goals, the *NSPI* centers on three pillars: preparedness and communication, surveillance and detection, and response and containment (NHSC, 2005, p. 2).

Preparedness and response activities focus on: 1) expanded production and stockpiling of vaccines, antiviral and medical supplies; 2) vaccine and antiviral distribution plans; 3) public communication and education; 4) and continued research and development of medicines and vaccines (NHSC, 2005, p. 4). For example, concern over an Avian Flu pandemic led to development of a vaccine using the current strain of H5N1 that offers protection in the early stages of a pandemic. Efforts are also underway to license additional egg-based influenza vaccine manufacturers to increase domestic vaccine manufacturing capacity and accelerate efforts to develop cell-based influenza vaccines and supporting infrastructure. These efforts support a goal of a 20-million course vaccine stockpile by 2009, which would be used to immunize healthcare workers, first responders, and at-risk populations in the early stages of pandemic. Combined, these efforts provide surge capacity to produce the remaining 240 million courses within 6 months of an outbreak. Other efforts include research and development of dose-stretching technologies and the use of adjuvant and other antiviral products. Finally, communication efforts target public education regarding pandemic risk and individual assistive behavior (Leavitt, 2005).

Surveillance and detection activities focus on the development and implementation of domestic and international surveillance systems to detect outbreaks anywhere in the world. These systems facilitate rapid reporting and implementation of measures designed to slow or stop the spread of the infection across domestic and international borders (NHSC, 2005, p.7). In September 2005, the US launched the International Partnership on Avian and Pandemic Influenza, a consortium of 88 countries and 9 international organizations that collectively shares information and samples of emergent viruses for study and analysis. The 2005 National Bio-Surveillance Initiative is designed to enable rapid detection of outbreak of disease in humans or animals, confirm the size and characteristics, communicate vital information, and respond to outbreaks (Bush, 2005).

Response and containment activities focus on mechanisms to leverage public and private health-surge capacity, to sustain vital infrastructure, services, and our economy, and to inform the public (NHSC, 2005, p. 8). Response to a pandemic will come from all levels of government, with state planning and response being key to containment. To date, all 50 states have plans outlining state surveillance strategies, vaccine and antiviral distribution and use, restricted movement plans, and public communication. Essential medical equipment and supplies are being purchased and added to the national stockpile to support a surge in hospitalization requirements that will come with a pandemic (CBO, 2005, p. 15).

Vaccines (Developmental Problems)

The development of vaccines is the focus of US national preparedness to counter pandemics or bio-terrorist attacks. When compared to the huge market for therapeutic drugs, however, the US vaccine market is relatively small (Gottlieb, 2004, ¶ 1) with just a handful of suppliers. The US government is the primary or sole buyer of certain vaccines. Not long ago the dwindling number of manufacturers and continuing shortages of flu and some childhood vaccines raised serious concerns about the future of the industry (Offit, 2005, ¶ 9). Recently, however, analysts have noted an upswing in the market, credited in part to “breakthroughs in technology” (Costello, 2007, p. A1).

Developers of new vaccines face significant technical, financial and legal challenges. Scientists must invest years or even decades in the search for new technologies to create vaccines for diseases, such as HIV and malaria, which do not respond to traditional live or attenuated virus approaches. The "very high sunk costs" of this research & development (R&D), plus lengthy and expensive Food and Drug Administration (FDA) approval procedures (Coleman, 2005) and the "functional cap" on prices set by the US government (USG) as a major buyer (Offit, 2005) pose daunting financial obstacles for manufacturers. Additionally, society demands higher safety standards and fewer side effects for vaccines than for therapeutic drugs, because the former are generally given to healthy, rather than sick individuals (Offit, 2005). Thus, liability issues and litigation expenses greatly increase the overall R&D costs for vaccines.

Current advances in biotechnology promise to address some of these problems. The newer DNA, RNA and "post-genomic" approaches to the immune system may eventually allow for more rapid development of innovative vaccines (Landry & Heilman, 2005), and DNA vaccine platforms are expected to offer greater economy of scale in development and production (NY Times, 2006), all of which will lead to greater profitability. Newer technologies also may be used to minimize adverse effects, i.e., through vectored vaccines (Landry & Heilman, 2005), and correspondingly reduce liability concerns and litigation.

Recent acquisitions of vaccine companies by pharmaceutical giants, such as Pfizer, have been hailed as a sign of resurgence in the vaccine market (NY Times, 2006). As long as innovative vaccines move through the pipeline, find new buyers, and command higher prices (e.g., Merck's new Gardasil vaccine for the HPV virus), we may expect the industry to strengthen. (Offit, 2005), however argues that mergers have not always proved beneficial to the industry, as vaccine divisions of large drug companies must "compete for resources with drugs and most often lose," because drugs are inherently more profitable than vaccines, requiring repeated doses compared to just a few doses of a vaccine in a patient's lifetime.

At present, the number of vaccine producers remains small, with many vaccines of interest to the government manufactured by sole suppliers. Thus, to meet public health and bio-defense requirements it may be necessary for the USG to continue providing incentives for R&D to encourage the production of vaccines with greater shelf life and to work with the FDA to accelerate the approval of new vaccines (Danzon & Pereira, 2005).

EMERGING TECHNOLOGY

Bionanotechnology

Bionanotechnology is a rapidly advancing area of scientific and technological opportunity. It is a branch of nanotechnology that uses biological starting materials, biological design principles or has biological or medical applications. The US leads the world in nanotechnology research, one of the great frontiers in science and engineering.

The challenges of bionanotechnology are daunting, as it involves industrial products and processes in the realm of nanometers or one billionth of a meter (Feder, 2004). Researchers have now determined the feasibility of tailoring molecules and manipulating individual atoms to design materials, medicines, electronics and machines at the tiniest most fundamental level, or nano level. However, at the nano level materials take on new properties that make the application of such materials challenging.

Despite the challenges, bionanotechnology is an attractive area for research and development. The knowledge base developed in biotechnology has much to offer with its understanding of life at the molecular level and how to commercialize living organisms. The fusion of engineers and scientists skilled in biotechnology and nanotechnology will provide an opportunity to create and commercialize bionanotechnology products.

Today, researchers are already using bionanotechnology for a variety of purposes to include the creation of biomolecules with new functions for molecular modeling, the creation of implantable artificial organs, and the development of bionanomachines. One example of a bionanomachine is a scaffold which is a tiny microscopic self-assembling device that assembles itself inside the body and could point the way to regeneration of spinal cords and the ability to grow tissues ranging from bone cartilage to blood vessels. This technology can also be used to build the biological detection system capable of accurately testing the presence of biological agents such as anthrax, smallpox and Severe Acute Respiratory Syndrome (SARS).

The scientific community anticipates a variety of applications for this rapidly developing technology. Bionanotechnology can be used to improve drug delivery, create self-assembling silicon structures for the tiniest of computer chips and for biodegradable absorbent wipes to detect bacteria, viruses and other dangerous substances. Scientists are also reporting the development of a nanoemulsion composed of detergents, vegetable oil and water to inactivate the Ebola Virus.

Despite the opportunities bionanotechnology offers, there is growing concern that the US is not paying enough attention to the environmental, safety and health risks posed by nanoscale products. As in other areas of the biotech industry, there is a concern about introducing bioengineered organisms into the environment. These concerns are valid, and there is some evidence that engineered nanoparticles have had adverse effects on the health of laboratory animals. Regardless, approximately 300 consumer products already contain nanoscale ingredients including several foods and many cosmetics with little or no research to document their safety (Weiss, 2006, p. A01). As in other areas of biotechnology, bionanotechnology offers great opportunities in the 21st Century. At the same time it must be balanced to ensure there are no unintended consequences brought about by its application.

BIODEFENSE

Bioterrorism

Bioterrorism is defined as “the use of pathogens or toxins against human, animal or plant populations by a terrorist group to achieve political, social or religious aims” (Pilch, 2002, p. 274). Recently, bioterrorism has been increasingly seen as a major potential threat to US interests. One reason for this is, it is seen as the “poor man’s atomic weapon” (Miller, Engelberg & Broad, 2001, p. 316). Biological weapons are easier to acquire then nuclear weapons with biological agents, technical expertise and production equipment more readily available.

A problem with identifying bioterrorism is that natural outbreaks of pathogens occur around the world frequently. Differentiating what is a natural occurrence from one that is man made can be difficult. That is of course, unless the attack is as obvious as the anthrax attacks in Washington D.C. in 2001. Additionally, there are a large number of pathogens in the over 1,000 culture collections in the world (Pilch, 2002, p. 275). Many of these collections are relatively secure, but the security of some is in doubt.

The first major case of bioterrorism in the US was conducted in 1984 by followers of Bhagwan Shree Rajneesh, in Oregon. Salad bars in local restaurants were contaminated with *salmonella,* and 1,000 people were poisoned (Miller, Engelberg and Broad, 2001, p. 15). The most well known case of bioterrorism in the United States involved powdered anthrax being mailed to members of Congress and prominent media personalities in 2001. There were 18 confirmed cases of anthrax, five deaths, and no person has ever been found responsible (Leitenberg, 2002, p. 33).

The technical capability to develop a range of pathogens and link them with dispersal means and a delivery system is complex. A recent report stated that "the unavoidable conclusion is that only a nation-state could conduct a bioweapon attack" (Stolar, 2006, p. 2). The major concern is not necessarily use of a bioweapon by a state, but the transfer of bioweapons or biotechnology to a terrorist group for their use.

The Centers for Disease Control and Prevention (CDC) maintains a list of biological agents it considers the most likely threats to US interests. It bases this list on an agent's toxicity, ease of production and delivery, transmissibility and potential impact on public health (Pilch, 2002, p. 270). The Class A (greatest threat) agents are smallpox (V*ariola major*), anthrax (*Bacillus anthraxis*), plague (*Yersinia pestis*), botulism (Botulinum toxin), tularemia (*Francisella tularensis*), and filoviruses and arena viruses. All of these agents have high toxicity, spread relatively easily and would have an enormous impact if used as part of a bioterrorist attack. There are also a variety of agents that have a high probability of use, but with limited impact such as food and waterborne pathogens like *Salmonella* and *Shigella*. They are relatively cheap, easy to acquire and produce, and are generally non lethal. (Pilch, 2002, p. 273). The attack by the Rajneeshees was an example of the use of agents of this type.

There is evidence that Al Qaeda and affiliated groups are interested in obtaining bioweapons. However, there is little evidence that they have made significant advances towards this goal. Documents found in Afghanistan and testimony from captured Al Qaeda operatives indicate an interest in bioweapons, but not to the exclusion of other operational activities. The current evidence regarding Al Qaeda and bioweapons is circumstantial and a good summary is the testimony in 2002 by General Franks when he stated, "We have seen evidence that Al Qaeda has a desire to weaponize chemical and biological capability, but we have not yet found evidence that indicates that they were able to do so" (Leitenberg, 2002, p. 26).

Perhaps the most likely way a terrorist group could obtain a bioweapon would be to purchase it from a country with weaponized agents. Currently, the most likely source would be to buy weaponized agents from the former Soviet Union. Both the US and Russia are aware of this and there are joint efforts to control these agents. As a policy action to counter potential Weapons of Mass Destruction (WMD) threats, including biological threats, the USG developed Project Bioshield.

Project BioShield

President George W. Bush signed the Project BioShield Act of 2004 (Project BioShield) into law (Public Law 108-276), on July 21, 2004, as part of a broader strategy to defend America against weapons of mass destruction. The purpose of Project BioShield is to accelerate the research, development, purchase and availability of medical countermeasures, including therapeutics, vaccines, medical devices and diagnostics to protect Americans against the effects of chemical, biological, radiological, and nuclear (CBRN) agents (DHHS, 2006).

In Project BioShield, Congress gave the Secretary of the U.S. Department of Health and Human Services (HHS) enhanced authority to develop and acquire medical countermeasures, including: 1) Use of certain procedures regarding research and development activities that involve qualified medical countermeasures; 2) Authority to use the Special Reserve Fund (SRF) for the acquisition of medical countermeasures for the Strategic National Stockpile; and, 3) and Emergency Use Authorization (EUA) for medical countermeasures (DHHS, 2006).

During the first two years following enactment, Project BioShield authorities expedited Review and Award Authorities by awarding grants for research and contracts for development and production of therapeutics for the most serious biological threats as determined by the HHS/Centers for Disease Control and Prevention (CDC). Project BioShield authorities also appointed three key Associate Directors to support HHS/National Institute of Health (NIH)/National Institute of Allergies and Infectious Diseases (NIAID) biodefense and radiation/nuclear medical countermeasure initiatives. It also awarded contracts using the SRF, most within 15 - 21 months after the Office of Management and Budget (OMB) approval. It also awarded contracts using the SRF, most granted within 15 - 21 months after the Office of Management and Budget's (OMB) approval. Finally, it authorized the emergency use of Anthrax Vaccine Absorbed (AVA) for prevention of inhalation anthrax in at-risk Department of Defense (DoD) personnel (DHHS, 2006).

Despite its initial accomplishments, Project BioShield has been perceived as weak, chaotic, and bereft of significant progress. Project BioShield has failed to secure the cooperation of big biotechnology firms to participate in the anti-bioterrorism program. Uncertainty and low profit margins make it hard to attract higher margin businesses (Chao, 2005). Thus, the government has had to depend on small, financially shaky biotechnology companies for the development of needed medical countermeasures. Additionally, HHS lacks the legal authority to use public funds extensively to shore up companies (Gillis, 2006). Moreover, some companies have complained of poor implementation of the program (Lipton, 2006), and that politics has adversely affected the treatment of the pharmaceutical industry (Pringle, 2006). While Project BioShield is a good first step in creating a broad strategy to defend the US against weapons of mass destruction attack, it has not met all of its intended objectives.

AGRICULTURAL

Agriculture

America leads the world in Agricultural Biotechnology (Ag Biotech), an industry dominated by seed and chemical companies. The Ag Biotech market is often mischaracterized by overemphasis on fertilizer and agricultural chemical companies that have divisions in the Ag Biotech market. The top four companies of the Ag Biotech market (*sensu stricto*) are Syngenta ($8.1 billion in revenues in 2005), Monsanto ($7.3 billion in revenues in 2006), DuPont Agriculture & Nutrition ($6.3 billion in revenues in 2005), and Dow AgroSciences ($3.3 billion in revenues in 2005) (Plunkett Research, 2007).

Ag Biotech accounts for less than 5% of the U.S. market, but worldwide it was over 12% in 2005. Ag Biotech is crucial to China's future development; the "Special Foundation for Transgenic Plants Research and Commercialization" (Plunkett Research, 2007) was established by the Chinese government to oversee foreign research organizations and companies. Ag Biotech made up 37% of the Chinese market and will undoubtedly be critical in feeding their future

population (Marketline Business Information Center, 2007, ¶ 1). Ag Biotech is growing in Europe; the number of acres of GM corn planted in France increased ten-fold from 2005 to 2006 (Ag Biotech Europe, 2007, ¶ 1). The U.S. is still the world leader in GM crop production, followed by Argentina, Brazil, Canada, India, and China (Countries Growing GMO, 2007, ¶ 1).

GM organisms are ones whose genetic material has been changed in a way that could not occur in nature through natural recombination or crossbreeding. It typically involves moving genes from one species into another species using specialized laboratory techniques. In the case of plants, the products of traditional crossbreeding techniques are not normally considered to be GM even though they may contain genes from different species.

Ag Biotech produces a broad spectrum of products including pharmaceuticals, biodegradable materials, and enzymes. Researchers are currently working on traits for tolerance to drought, temperature, and salinity to allow crops to grow in marginal environments (Countries Growing GMO, 2007). Herbicide and insect resistance traits will continue to be pursued since 25% of food crops are lost each year to insect damage, and weed competition (Countries Growing GMO, 2007).

Pesticide use has been reduced 15% and herbicide use by 4% since 1996 (Brooks & Barfoot, 2006, p. 139). GM crops have led to reduced or no-tillage farming. This reduces topsoil erosion and increases the amount of organic material in soil, providing better environmental conditions for insects, birds, and small mammals. It locks carbon dioxide in soil and, combined with reduced fuel use due to less plowing and spraying, has reduced greenhouse gas emissions by 9 billion kg per year, equal to removing 4 million cars from roads (Brooks & Barfoot, 2006, p. 139). Over the last 50 years, traditional agricultural practices have resulted in the loss of 20% of the world's topsoil and clearing of 33% of the world's forests (Cockburn, 2004, p. 209).

GM crops produced economic benefits estimated at over $27 billion in reduced farm costs between 1996 and 2005 (Brooks & Barfoot, 2006, p. 139) and resulted in additional economic benefit to consumers and farmers. Studies show farmers who could not grow GM crops are worse off; consumers who don't have access to/chose not to buy GM products are worse off economically (Moss, Schmitz & Schmitz, 2006, p. 46). Scientific and other scholarly evidence can only do so much to resolve the controversies surrounding GM plant products. As the world population grows, urbanization increases, and associated environmental pressures mount, the future of agriculture will depend more and more on biotechnology as we attempt to provide a secure, nutritious, and environmentally sustainable food supply for the world.

Biofuels

The siren call of ethanol is irresistible; it's homegrown, renewable and less polluting than gasoline. In 2006, about 5.5 billion gallons were produced in the US - a doubling of production (RFA, 2007). This number appears high, but it represents less than 5 percent of the US gasoline market. A review of ethanol's production, benefits and consequences is required to determine if it is a true economic and environmental alternative for energy.

Ethanol can be made from any feedstock, however about 95 percent of the ethanol produced in the US is derived from corn due to its low cost and high yield. On an equivalent energy basis, a gallon of ethanol from corn costs twice as much to produce as a gallon of gasoline (Yacobucci, 2007, p. 12). Ethanol's production cost is driving research to convert starch into sugar from inedible plants, known as cellulosic conversion. In January 2007, US Agriculture Secretary Johanns announced a $1.6 billion plan for research on cellulosic conversion (Williams,

2007). A month later, Energy Secretary Bodman announced $385 million in grants to six recipients for cellulosic conversion research (Stevens, 2007). Investors are following government's lead and directing more funding into cellulosic technology (Barta, 2007, ¶ 1).

A benefit of ethanol is improved air quality because it produces less green house gases than gasoline. Most gasoline sold in the US today consists of 10 percent ethanol in order to comply with Clean Air Act requirements. Further, American car manufacturers produce "flex fuel" vehicles that run on gasoline and E85 (85 percent ethanol, 15 percent gasoline) in order to meet targets set by the Corporate Average Fuel Economy Act. However, of the nearly 165,000 fueling stations nationwide, only 1,166 sell E85, mostly in the mid-west near ethanol producers (NEVC, 2007). Unfortunately, the physical properties of ethanol prohibit the use of gasoline pipelines for ethanol. Another benefit is that ethanol production may enhance US energy policy. The top two ethanol producers are the US and Brazil; each produces 35 percent of the world supply (NEVC, 2007). President Bush launched an initiative with Brazil to create an alliance of ethanol producing countries (Baker, 2007).

The rush to produce ethanol is resulting in unintended consequences. In 2006, 18 percent of the US corn crop was used for ethanol production (Standard and Poor, 2007). By 2008, half of the US corn crop could be so used (Carey, 2007). Corn prices doubled from $2 a bushel in January 2006 to $4 a bushel in February 2007 (NCGA, 2007). The President of Cargill, a large US agribusiness, cautioned "the agriculture sector from becoming too focused on biofuels as it will have unintended consequences on food prices," (Cameron, 2007). Increased ethanol production is also resulting in more acres being planted for corn, perhaps as much as 10 million additional acres (Tilman, 2007, ¶ 1). The Department of Agriculture announced 1.4 million acres in corn states dropping out of the Conservation Reserve Program, which is designed to conserve low-quality farmlands (GREEN, 2007, p. 4).

The US rush to ethanol as a renewable energy source is popular and is creating many changes. However, the growth of ethanol is retarded by the inability to cheaply convert non-edible plants into sugar, then ethanol, and to economically transport ethanol from producers to consumers. In order for ethanol to become a major renewable energy source in the US, these challenges must be overcome.

Cloning

Cloning is safe, but the word "cloning" elicits a negative visceral reaction on the part of many Americans. Cloning is a means of producing identical genetic copies of a gene, cell, or organism. There are two dominant means of cloning. In embryo twinning, individual cells are separated from an early embryo and are allowed to divide and develop in a Petri dish. The newly developed embryo is then surgically inserted into a surrogate mother. Somatic cell nuclear transfer uses somatic cells, which are any cells other than reproductive cells (sperm and egg). The nucleus of a somatic cell is removed and inserted into an egg cell whose nucleus was previously removed. When treated by chemicals, the egg cell is transformed into a fertilized zygote, and after developing into an embryo it is surgically inserted into a surrogate mother. Dolly the sheep was cloned by the latter process. The result was that Dolly's DNA was an exact replication of the DNA contained in the original somatic cell.

Despite the success of duplicating the desired DNA, there are concerns about the use of cloning livestock and other purposes. The most prominent criticism is that cloning is unsafe. Dolly the sheep was the lone survivor of a process where only 29 of 277 of the cloned embryos

developed normally and survived to birth. Of those, the incidence of deformities, enlarged kidneys, or abnormally large birth weights was extremely high.

Cattle are cloned for their milk-producing capability, but only their conventionally bred offspring can be used as milk producers. The clones are far too valuable to be used as commercial "milkers" and only their progeny are inexpensive enough to be put on the line. While currently too expensive, the benefits to cloning are already apparent. Among the most vocal of the proponents were farmers and ranchers; generally, they see cloning as the next logical step in the food industry.

The other side of the cattle business, dairy producers, supports cloned milk producing cows. A Pew/FDA workshop determined that there was "… almost no difference between milk from cloned cows compared to non-cloned cows," and that "… individual proteins, fats, lactose and total solids were very comparable between Holsteins, cloned Holsteins, a brown Swiss and two crosses" (Pew, 2006). Beyond the apparent benefits of taste, quality and uniformity, there are positives for the herd. Cloned animals of "hardy stock" are less susceptible to disease, better able to withstand harsh climactic changes, and prone to exhibit better social behavior. The primary reason cloning for food production hasn't moved forward is that it is a distasteful concept to many people.

ETHICAL CONCERNS

Over the centuries, scientific advancements have often caused society to ask whether man, in using new technologies, was contravening nature or trying to play God. Even the innocuous umbrella was eschewed by our Puritan forebears as "unnatural." But, just as umbrellas, bicycles, air flight and organ transplants are now commonplace and accepted, we can expect that most of today's controversial biotechnology breakthroughs, if proved successful and beneficial to society, will eventually become part of the texture of human life, deemed no more unnatural than a daily bath or a microwave meal.

Biotechnology and the scientific advances achieved using the tools developed in this discipline have "inextricably linked the promise and peril of our time with the promise and peril of modern science" (Kass, 1985, p. 1). The new biotechnologies "have often brought with them complex and vexing moral and social difficulties, and the scientific discoveries themselves raise disquieting challenges to traditional notions of morality or of man's place in the world" (Kass, 1985, p. 1).

The greatest area of controversy in the US today continues to be the ethics of using human embryonic stem cells (HESC) for research on and treatment of disease. Americans line up on either side of this issue, depending on their beliefs regarding the humanness of a newly formed embryo. Just as the importance of a woman's right to choose may tip the balance for the undecided on abortion, the potential quality-of-life-benefits of HESC for sufferers of Amyotrophic Lateral Sclerosis (ALS), Alzheimer's or Parkinson's has won over some support for HESC research even from among the ranks of skeptics. Thus, despite the federal ban on funding, several states have bankrolled their own independent programs. Medical researchers, for their part, try to work around federal funding restrictions, and seek to use hard scientific facts to make their case about the ethicality of HESC research.

GM organisms provide great promise in the areas of agricultural food production, food safety, environmental protection, and nutrition. Although there is wide support and acceptance in the US for GMs, worldwide support is more elusive. Areas of concern include issues related to

trade, food safety, and danger to the environment from genetic drifts. Who is the responsible authority to ensure safe food and feed? Can the GMs be traced accurately? These and many other questions present ethical dilemmas that can appear to sacrifice safety and choice for production and efficiency.

Biotechnology has enabled the field of personalized medicine to appear on the ethical landscape. Technological advances in understanding an individual's genetic predisposition have revolutionized the physician-patient relationship, streamlining care and eliminating waste and inefficiency. Unfortunately, the downside to our ability to better anticipate future conditions can be discrimination by insurance companies or employers on the basis of genetic profiling.

A further area of ethical concern is the patenting of organisms and genetic codes, specifically, where patents on "biological materials and the traditional knowledge of how to use those materials" may deny "researchers in developing countries…further access to their own biological resources," or where patents granting the holder "monopolies over seeds and plant varieties [could create] serious implications for agriculture and food security" (Grace, 2006, p. 198). Critics also question the ethicality of entities, such as NIH, patenting human cell lines "containing [an individual's] unmodified DNA" for use in scientific research, without commensurate compensations for the donor (Grace, 2006, p. 199).

Perhaps the greatest challenge, though, is a result of breaking the genetic code. We now have the ability to change, either radically or minimally, the living things that we rely upon for our existence; we can even change ourselves as a species. It is an awesome power fraught with ethical dilemmas that we are only now beginning to voice. The embryonic stem cell debate is perhaps the most well known; many other debates are also raging, such as those concerning genetically enhancing food crops and controlling information related to an individual's genetic makeup. While all industries face ethical questions, those facing biotechnology are perhaps more acute as they drive to the very meaning of *Homo sapiens* as a species. These dilemmas must be addressed in order for the industry to continue to grow.

CURRENT CONDITIONS / CHALLENGES / OUTLOOK

As we consider the potential ethical issues and the myriad uses of biotechnology discussed above, we must also look at where we are in a more general sense in terms of the current conditions, pending challenges, and the outlook for the future of the biotechnology industry.

Current conditions in biotechnology enable start-up companies to compete with giant pharmaceuticals or agri-business conglomerates in the arena of new ideas, whether those ideas are new ways to produce large-molecule cancer drugs or salt- and drought-resistant grain. Despite this innovative freedom, the challenges facing the industry today are numerous and range from legislative restrictions on various aspects of the industry to the difficulty in recruiting qualified people to conduct basic research.

Threats to intellectual property rights and patent challenges from international generic drug companies add to the economic barriers for the industry, and shortages of qualified people to run research labs, bioreactors and manufacturing facilities affect all the companies involved. Aside from industry giants such as Monsanto or Merck, most biotech companies are small (less than 50 employees) and have yet to realize any profit from their products. (BIO.org, 2007)

Still, with all those challenges, the outlook for the industry is very promising. The importance and value of the biotechnology industry will only increase as new developments and products are introduced. Leadership in biotechnology, which the US enjoys at the moment, will

increasingly be a strategic national interest. To maintain this leadership, the US must focus efforts on several critical areas including education and intellectual property rights.

Education

The growth of the biotech work force from 103,000 in 1994 to 187,000 in 2004 is indicative of the growth of the industry in general (BIO, 2007). The innovative intensive nature of the industry requires a well-educated work force of scientists and technicians. For the industry to continue to grow, it must continue to attract qualified researchers. Unfortunately, several US companies stated during our site visits that it is increasingly difficult to recruit qualified employees due to the declining number of US graduates in life sciences and limited number of international graduates allowed to work in the US. Several Indian companies echoed the same sentiments with regard to attracting and retaining highly educated employees.

The number of degrees awarded by US universities has increased by 67 percent from 1971 through 2004. However, the number of degrees awarded for biological and life sciences has been decreasing. In fact, from 1996 through 2003, the number of biological and life sciences Bachelor's degrees awarded dropped by 6.2 percent, Master's degrees by 2.4 percent, and Doctoral by 3.3 percent (Goan and Carroll, 2006). This decrease is due to several factors, including the poor quality of science and math education in US primary and secondary schools and students' perception that science careers are not as rewarding as careers in business or liberal arts (Staples, 2006).

The state of primary and secondary education has long concerned US policy makers. Many federal and state initiatives have been implemented to attract students to math and science. Recently, private foundations and universities have partnered with the biotech industry to foster educational outreach programs. For instance, the Venter Institute operates the Discover Genomics mobile lab, which visits secondary schools in the Washington, D.C. area (Rasicot, 2007); the Broad Institute offers summer internships to high school students in the Boston, MA, area; and the Biotechnology Industry Organization offers teacher workshops in the Philadelphia, PA, area. These partnerships between industry and education may lure additional students to the biotechnology world.

The US is not alone with regard to educational challenges. By some accounts, up to half of the students in India who graduate with degrees in math and science are unemployable given their low technical skills. India possesses some world-class universities. In particular, Jawaharlal Nehru University and Indian Institute of Technology graduates are highly sought by biotech companies due to their excellent technical skills. The challenge for India is to improve its higher education system so that graduates from more of their colleges are prepared to successfully enter the biotech workforce.

Indeed, the growth of the biotech workforce has been fueled in large part by international students seeking employment in the US. Under the Immigration and Nationality Act, US companies may employ a foreign national for up to 6 years in a job that cannot be filled by a US citizen, provided the foreign national possesses an equivalent education. Most of these jobs are related to math, science and engineering. The number of visas for this program was reduced in 2006 to 65,000 from a high of 107,500 in 2001. In 2005, 44 percent of these visas were granted to workers from India (U.S. CIS, 2006). While the quota rapidly fills every year, the number of petitions has been declining since 2003. The petition decline has been attributed in part to the Iraq war and more intense scrutiny of foreigners entering into the US (Cowen, 2003).

The decrease in US life sciences graduates and the decline in temporary worker visas are worrisome indicators for the US biotech industry. If the US biotechnology industry is to continue growing and maintain its technological lead, it must have a continuous infusion of talented researchers. In addition, the intellectual property rights of these researchers must be protected to maintain the economic viability and healthy competition of the market place.

Intellectual Property

The protection of intellectual property is the heart and soul of the biotechnology and biopharmaceutical industry. Enforceable patent protection is vital to an industry that may spend nearly a decade and hundreds of millions of dollars to produce a single product. In order for the private sector to recoup their investment, they need profit margins to be assured by patent protection for a significant number of years. If the industry is to grow, then the private sector needs to secure patent protection that will enable profits in excess of their initial investment. This excess is required to fund new research and development of future products.

In a recent ruling by the *US Supreme Court, KSR International v. Teleflex Incorporated (2006)*, conventional understanding of US patent law was challenged. Patents offer protection for unique inventions but do not provide similar protection for "obvious" improvements or "obvious" combinations of patented technology. The heart of the debate centers on what constitutes an "obvious" improvement vs. a unique invention that can be protected by patent law. What would an expert in a specific field deem as an "obvious" improvement? The October 2006 ruling by the US Supreme Court narrows what can be protected and broadens the definition of "obviousness". To the US biotech industry, this is problematic since firms often rely upon incremental improvements to an existing invention to provide continuing cash flow and profitability. As mentioned above, the completely new or so called "big-bang" inventions often take years and incredible sums of money to develop into a commercially viable product. Smaller levels of invention around an existing product are much faster and cheaper to develop. Losing broad patent protection is anathema to many US biotech firms as it erodes current and future profitability.

India, on the other hand, has invested heavily in biotech products that are off-patent – primarily generic drugs – and the current court ruling opens the door for additional generics to be created without violating patent law. The anathema for the US is a boon for India's well-heeled emerging biotech companies. This ruling is likely to encourage more aggressive challenges of US patent law by biotech companies across the globe and portends costly litigation for US firms as they try to defend their invention against hungry biotech companies seeking to gain market share in the US and abroad.

As these issues of education and intellectual property rights gain attention, many will look to governing bodies to provide regulation to protect various countries and/or companies as they seek to gain economic advantage from their products.

ECONOMICS AND REGULATION

Biotech in the US

"In 2005 the biotech industry generated $51 billion in US sales. It is one of fastest growing US industries and created 40,000 jobs from 2001 to 2004" (Timmerman, 2007). Still

young, the industry is dynamic and converging with many other industrial sectors and markets. Biotech has the potential to be an engine for US economic growth similar to the chemical industry in the 1950s-70s. As the US enters the 21st Century it is the undisputed leader.

Armed with information age tools and sophisticated software, the industry has been able to manipulate life at the molecular level like never before (Nanooze, 2007). The result has been a rapid rate of scientific discovery in life sciences and the commercialization of biotechnology. A mixture of private and government-funded research coupled with a market economy, entrepreneurial spirit, superb academic institutions and a robust capital market, has propelled the US biotech industry.

The most progress has been made in the human health care industry. The human health care industry, with the robust infrastructure of labs, businesses, academic institutions, lab technicians, chemists, microbiologists, and doctors, has made the biotechnology industry a core part of the human health care sector. As a result there are more than 300 biotech drug products in clinical trials targeting more than 200 diseases and illnesses. In 2003 the total revenues generated by the healthcare sector totaled $39 billion (BIO, 2007).

In agriculture, Biotech has made substantial progress by increasing yields and reducing costs. GM organisms increased crop yields, reduced pesticide use and are even being used to replace chemical-based resources used in manufacturing processes (fuel, plastics and textiles). The US is the world leader in GM crop production. In 2003 eleven varieties of biotech crops were adopted by US growers increasing crop yields by 5.3 billion pounds, and lowering production costs by $1.5 billion, for a combined net economic gain of $1.9 billion. Despite progress, biotech in agribusiness is held back by the lack of wide-spread domestic and international acceptance. GM organisms face hurdles such as government barriers to entry and consumers who fear the unintended consequences of releasing new organisms into the environment. As a result, the agricultural industry has taken a cautious approach to expansion.

In addition, a new segment of the biotech industry is emerging – industrial applications. Market conditions and technological advances have created interest in using biotechnology products in manufacturing and energy. Consumers are demanding environmentally friendly materials, and high oil prices have created a demand for non-petroleum-based resources. Large chemical makers, such as Dow Chemical, DuPont and Chevron-Texaco, are forging partnerships with biotech companies to develop new resources that can be used for manufacturing and energy production. Some examples are biofuels, textiles, ethanol, compact disks, or crops used to replace petrochemicals in the manufacturing process. Academic institutions are experimenting with microbes and living organisms to replace silicon based computer chips.

While the use of biotechnology in manufacturing is still in its infancy, the most advanced segment in biotech remains the human healthcare sector. As a result of the successful application of biotechnology in healthcare, multiple other industries are seeking to leverage the power and potential of biotechnology. Most are in the emerging phase, but all demonstrate tremendous growth potential both in the US and abroad.

Biotech in India

The Indian biotechnology industry has changed dramatically since the establishment of its first biotech company in 1978. Less than thirty years later, the biotechnology industry is over 280 companies strong and engaged in every biotech sector (Biotech Week, 2007, p. 41). A joint industry study of Indian biotech-related companies by BioSpectrum and the Association of

Biotechnology Led Enterprises (ABLE) in 2006 divides the industry into various segments: 72.2 percent biopharma; 11.04 percent bioservices; 9.17 percent bioagriculture; 5.75 percent bioindustrial; and 1.84 percent bioinformatics (Mergent, 2006, p. 19). Exports are valued at $747.87 million and are 51.4 percent of the market; biopharma accounts for 74 percent of exports, followed by bioservices at 21 percent, bioinformatics at three percent, with both bioindustrial and bioagriculture at one percent (Mergent, p. 19).

The Indian biotechnology industry is growing at a faster rate than other Indian industries. The BioSpectrum and ABLE industry study estimates Indian firms will grow from one percent of the global biotech industry in 2004-2005 to almost ten percent by 2010 (Mergent, 2006, p. 19). In 2006, India's biotechnology industry was $1.07 billion of a global biotech industry of $54 billion (M2 Presswire, 2006, p. 1). Growth reached 37.42 percent in the Indian biotech sector for 2005-2006, with individual corporate profits of companies exceeding 117.5 percent (Mergent, p. 3 & 5). RNCOS's 2006 Indian Biotechnology Market Outlook report estimates it will likely reach $5 billion by 2010 (M2 Presswire, 2007, p. 1). Key biotech growth areas cited include clinical trials, stem cell research, and genetically modified crops. In addition, biopharmaceuticals are poised to continue as the dominant segment in the Indian biotech industry.

There are many reasons why biotechnology firms and clinical researchers are interested in locating in India. India's population is genetically diverse. At the same time, it has homogenous communities, and its citizens suffer from similar diseases as Americans and Europeans. India's labor market advantages make it a prime outsourcing destination for biotechnology firms. RNCOS estimates a multinational company will save 30-50 percent by moving research and development to India (Drug Week, 2007, p. 359). KPMG documents clinical trial costs are one-tenth of Western levels, research and development costs are one-eighth of Western levels, and pharmaceutical production costs are fifty percent lower in India (Scott, 2006, p. 40). The cost savings associated with outsourcing research to India offers an opportunity to exponentially expand research output without additional investment.

India's Department of Biotechnology, established in 1986 as an agency of the Ministry of Science and Technology, is a powerful supporter of the biotechnology industry. Government investment in the biotechnology sector is a critical factor driving economic growth because of the large investment required to overcome industry entry barriers, to improve basic infrastructure, and to provide venture capital unavailable in the private sector. India's biotechnology industry has grown into an internal economic force because of the limited patent protections offered to foreign investors; indeed, India's dominance of the generics market initially depended upon it. Implementation of World Trade Organization patent protections in 2005 is increasing the likelihood of foreign investment in the Indian biotechnology industry and the proliferation of multinational corporations in India. India will need to observe the trade-related aspects of intellectual property rights or it will not gain the confidence of Western biotechnology companies. Diligent enforcement of new intellectual property laws will determine whether India is able to capitalize on its strengths and overcome its weaknesses to become a force in the global market. In addition to the impact of regulation on the producers, we are seeing significant impacts on the downstream users of biotechnology products. One specific example is the use of GM crops for Africa.

EU Trade Restrictions on GMO's and Their Strategic Impact on Africa

The overall global economic benefit of GM crops from 1996 through 2004 amounted to $27 billion, and 90% of the farmers benefiting from it were resource-poor, small-scale farmers in developing countries like Africa. GM crops are directly responsible for the alleviation of poverty for close to 8 million farmers (Africabio, 2007). While this is good news, the trade restrictions imposed by the European Union are severely limiting the benefits to the African people.

The EU imposes the "precautionary principle" to justify significant restrictions on importing GM crops. "When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established" (Appell, 2001). This means essentially that, since GM crops cannot be proven to *not* cause harm, the EU position is that the responsible thing to do is to prevent them from entering the EU. This position affects decisions that farmers outside of the EU make on what crops to grow. These restrictions are causing real harm - malnutrition and starvation in huge numbers in developing countries.

At a conference held in Washington in 1999, 25 US farming organizations warned their members against planting GM crops. Gary Goldberg, then chief executive of the American Corn Growers Association, declared, "It is clear that if farmers have any uncertainty over the availability of a market for GM crops next year or questions over segregation, cross-pollination or liability, they should consider planting alternatives" (Howard, 1999).

In southern Africa, crop failures have become a yearly occurrence since 2002. Sub-Saharan Africa faces acute malnutrition, which affects over 200 million people, and the region is the only one in the world where food production has actually declined over the past two decades. (Ochuodho, 2006, ¶ 1) Yet, with their people facing starvation and death in huge numbers, the government of Zambia refused the offer of food relief from the US because the corn was genetically modified. One reason was simple fear: Zambian leaders had been told that the corn causes a disease similar to AIDS/HIV in anyone who ate it. Another reason they refused to accept GM corn was fear that the GM corn would contaminate local crops and close the European market to Zambian exports. Droughts and crop failures have severely impacted Zambia lately, but that country is an exporter of corn to Europe; even during the famine of 2002, when over 3 million Zambians were starving! (Bodulovic, 2005, ¶ 1)

Even when there is a clear health benefit to genetically modified crops, not just improved crop yields or more appealing fruit or vegetables, the realities of the marketplace rule. Driven by consumer opinion in Europe and elsewhere, market forces will determine how biotech companies and American farmers will handle GM crops, and how the benefits of genetically modified food reach the people who need them most.

Regulation

The biotechnology industry is regulated by several domestic agencies including the FDA and the USDA. Internationally, the European Union regulates biotech through the European Commission and the Ministry for Agriculture, Fisheries, and Food Safety. These regulators attempt to act for the public good while ensuring the viability of the industry. However, tensions exist between these two responsibilities and are reflected in many of the current issues, including lengthy drug approval process, patent approval times, and stem cell research and therapy. As we

contemplate the consequences of regulation, we recognize some supports and controls must be applied to the developing industry of biotechnology.

POLICY RECOMMENDATIONS

Advances in biotechnology have brought a number of benefits to the world population, and the US strives to maintain its leadership in this area. There are challenges and issues relating to public education, intellectual property, R&D, and national security that have yet to be fully resolved. The following policy recommendations provide a basis to address these issues.

- The US Government needs to continue discussions through the Word Trade Organization to align US, European and other international patent systems, and support patent enforcement and compliance.
- The US Government needs to continue supporting US – India partnerships and collaboration in biotechnology that is beneficial to both countries. India's existing dominance in the production of vaccines has great potential for collaboration in the areas of bio-defense, bioterrorism, chemical-warfare vaccines and pandemic vaccines.
- Project BioShield should be restructured by reallocating funds from areas that are not generating significant interest from private industry and transferring these responsibilities to government agencies and laboratories.
- A bill has been introduced into the US Senate amending the Immigration and Nationality Act by increasing the number of temporary specialty occupation worker visas that may be issued annually. The Administration should work with Congress to raise the cap in order ensure a study supply of biotech scientists and technicians.
- The National Strategy for Pandemic Influenza (NSPI) outlines the coordinated actions required to prepare for and respond to a pandemic. To date, Congressional funding has not fully met plan requirements. The NSPI elements must be fully funded.
- The Department of Energy should sponsor a prize for development of a cellulosic process that converts, at low-cost, inedible and waste plant materials into a high yield of ethanol.
- The Environmental Protection Agency and Departments of Agriculture and State, with assistance from the Departments of Commerce, Energy and Interior, should conduct an analysis to identify the impacts of increasing corn demand on food security, environmental quality and US foreign policy.

CONCLUSION

The biotechnology industry is a key sector of the American economy. It employs hundreds of thousands of people and generates billions of dollars in revenue. It is a relatively young industry, coming into existence in the 1970's. Its future is bright with promise, but it also faces several hurdles in order to meet this promise.

In the past few decades, its products have revolutionized medicine. The industry has developed new vaccines and therapeutics for previously untreatable and emerging diseases. It promises the delivery of drugs tailored to an individual's genetic makeup in order to achieve optimal effect - something unthinkable 20 years ago. The medical advances in biotech are more important then ever as the growth of global trade and travel have also increased the threat of global pandemic, such as avian influenza.

Biotech has revolutionized agriculture. Genetically enhanced cotton in the US and India has reduced the amount of pesticide, fertilizer and water required to grow the crop. The promise of genetically enhanced food crops could result in a second green revolution capable of feeding the world's growing population. In some cases, medicinal and agricultural applications are merging as companies begin exploring ways to create human proteins using animals and plants as production factories. Finally, new and improved manufacturing processes and consumer products, such as biofuels, biodegradable plastics and nanoparticles are entering the marketplace, thus improving the quality of life globally.

The biotechnology industry is innovation intensive and requires a substantial number of qualified scientists and technicians to push the boundaries of science. Unfortunately, the US, like many countries, is not producing enough qualified personnel. While US needs are partially met by foreign nationals wishing to pursue research opportunities in the US, immigration policies are making it difficult to quickly recruit these researchers. The shortage of qualified personnel will continue to slow advances in the biotechnology industry.

The biotechnology industry requires long lead times to develop products. It is common for new drugs to take 10 to 12 years to develop given the requirements for clinical testing. A result is that many companies require several years, perhaps a decade, of capital investment without a financial return. This long lead time is difficult for investors to accept, especially when the guarantee of return is unknown.

Perhaps the greatest challenge, though, is a result of breaking the genetic code. We now have the ability to change, either radically or minimally, the living things that we rely upon for our existence; we can even change ourselves as a species. It is an awesome power fraught with ethical dilemmas that we are only now beginning to voice. The human embryonic stem cell debate is perhaps the most well known; many other debates are also raging, such as those concerning genetically enhanced food crops and control information related to an individual's genetic makeup. While all industries face ethical questions, those facing biotechnology are perhaps more critical as they directly impact the very meaning of life itself. These dilemmas must be addressed in order for the industry to continue to grow.

REFERENCES

Africabio, (2007, March 13), *The role of agricultural biotechnology in hunger and poverty alleviation for developing countries [Electronic version]*, retrieved from http://www.seedquest.com/news/releases/2007/march/18674.htm.

Agricultural Biotechnology in Europe, retrieved April 19 2007 from: http://www.abeurope.info/#

Appell, D., (2001, January), *The new uncertainty principle*, retrieved from http://www.biotech-info.net/uncertainty.html.

Baker, P., (2007, March 10), *US, Brazil Team Up to Promote Ethanol; For Bush, a Key Step in Boosting Regional Ties*, The Washington Post, retrieved March 12, 2007, from ProQuest database.

Barta, P., (2007, January 29), *Alternative Fuels Push May Inspire Some Better Bets*, The Wall Street Journal, retrieved March 12 , 2007, from ProQuest database.

Bartlett, J.G., Hayden, F.G., (2005), *Will It Be the Next Pandemic Influenza? Are We Ready?*, Annals of Internal Medicine, 143(6). 460.

BIO.org, (2007), *Tax and capital formation challenges for the biotechnology industry [Electronic version], retrieved May 14 2007 from: http://bio.org/tax/.*

BIO, (2007), *Biotechnology Industry Facts*, retrieved April 19, 2007, from Biotechnology Industry Organization: http://bio.org/speeches/pubs/er/statistics.asp?p=yes

Biotech Week Editors, (2007, Mar 7), *Biotechnology; Examine and Understand the Indian Biotechnology Sector*, Biotech Week, p. 41

Biotechnology Market, retrieved April 6, 2007 from: http://www.plunkettresearch.com

Bodulovic, G., (2005), *Is the European attitude to GM products suffocating African development?*, retrieved from http://www.africabiotech.com /pdf/Bodulovic.pdf.

Brooks, G., Barfoot, P., (2006), *Global Impact of Biotech Crops: Socio-Economic and Environmental Effects in the First Ten Years of Commercial Use*, AgBioForum, Vol 9 (3): 139-151

Bush, G. W., (November 2005), *Remarks by the President on the Administration's National Strategy for Pandemic Influenza Preparedness and Response*, retrieved 1 April 2007 from http://usinfo.state.gov/gi/Archive/2005/Nov/01-1635909.html

Cameron, D., Morrison, K., (2007, March 6), *Fuel or Food, a Debate Set to Rumble On*, Financial Times of London, retrieved March 12, 2007, from ProQuest database.

Carey, J., (2007, February 5), *Food vs. Fuel: As Energy Demand Devours Crops Once Meant for Sustenance, the Economics of Agriculture are Being Rewritten*, BusinessWeek, retrieved March 12, 2007, from ProQuest database.

Chao, P.A., (March 2, 2005), *The Structure and Dynamics of the Defense Industry*, retrieved March 28, 2007, from http://web.mit.edu/SSP/seminars/wed_archives_05spring/chao.htm,

Cockburn, A., (2004), *Commercial Plant Breeding: What is in the Biotech Pipeline?*, Journal of Commercial Biotechnology, Vol 10 (3): 209-223.

Collins, F., (2007), *Personalized Medicine: A new approach to staying well*, Boston Globe On-Line, retrieved March 19, 2007 via http://members.boston.com/news/globe/editorial_ opinion/oped/articles/2005/07/17/personalizedmedicine?page=1-3

Coleman, M. S., Sangrujee, N., Zhou, F., Chu, S., (2005, May/June), *Factors affecting U.S. manufacturers' decisions to produce vaccines*, Health Affairs, 24(3), 635, retrieved April 2, 2007, from ProQuest.

Congress of the United States Congressional Budget Office, (July 27 2006), *A Potential Influenza Pandemic: An Update on Possible Macroeconomic Effects and Policy Issues*, retrieved 23 March 2007 from http://cbo.gov/ftpdocs/72xx/doc7214/05-22-Avian%20Flu.pdf

Congressional Research Service, (2007), *Pandemic Influenza: Domestic Preparedness Efforts*, (RL33145), Washington, D.C., Government Printing Office.

Costello, D., (2007, January 28), *Vaccine industry is being revived: New technology, greater funding and higher profits are a shot in the arm for advances*, Los Angeles Times, [Home Edition], p. A1, retrieved April 2, 2007, from ProQuest.

Countries Growing GMOs, retrieved March 19 2007 from: http://www.gmo-compass.org/features/printversion.php?id=142

Danzon, P., Pereira, N. S., (2005, May/June), *Why sole-supplier vaccine markets may be here to stay*, Health Affairs, 24(3), 694, 3 pp, retrieved April 2, 2007, from ProQuest.

Department of Health and Human Services' Office of Public Health Emergency Preparedness, (July 31, 2006), Project BioShield: Annual Report to Congress (July 2004 through July 2006), retrieved March 1, 2007 from: http://www.hhs.gov/ophep/ophemc/bioshield/annualreport/ annualreport.html.

Drug Week Editors, (2007, Feb 9), *Market Analysis; India ramps up biotech funding*, Drug Week, p. 359.

Feder, B.J., (2004), *Doctors Use Nanotechnology to Improve Health Care*, The New York Times, November 01, 2004.

Ghedin, E., (2005), *Large-scale sequencing of human influenza reveals the dynamic nature of viral genome evolution*, Nature, 437. 1162-1166.

Gillis, J., (March 17, 2006), *No Hope for Stockpile of New Anthrax Vaccine by November*, The Washington Post, retrieved March 28 2007 from: http://projectdisaster.com/?m=20060321.

Goan, S. K., Carroll, C. D., (2006, May), *Degree Completions in Areas of National Need*, 1996-1997 and 2001-2002, retrieved May 15, 2007, from National Center for Education Statistics: http://nces.ed.gov/pubs2006/2006154.pdf

Gottlieb, S., Calfee, J. E., (2004, December 7), *Putting markets to work in vaccine manufacturing*, AEI, retrieved April 3, 2007, from http://www.aei.org/include/pub_print.asp?pubID=21659

Grace, E.S., (2006), *Biotechnology Unzipped: Promises and Realities*, Washington D.C., Joseph Henry Press.

Grassroots REenewable Energy Network (GREEN), (2007, March 19), *Production & Demand Skyrocket*, Iowa Renewable Fuels Association, Newsletter for Renewable Fuels Advocates.

Henderson, D., (1999), *Smallpox as a Biological Weapon*, Journal of the American Medical Association, Vol 281, No 22.

Hopkins Center for Civilian Biodefense Studies Symposium, (1999), *Fact Sheets*, retrieved 29 Mar 2007 from http://www.hopkinsmedicine.org/press/1999/February/990209.htm

Howard, J., (1999, November 25), *Groundswell of US farmers warn against GE crops*, retrieved from http://www.scoop.co.nz/stories/HL9911/S00179.htm.

Kass, L.R., (1985), *Toward a More Natural Science*, New York, NY: The Free Press.

Kortepeter, M., Parker, G., (1999), *Potential Biological Weapons Threats*, Emerging Infectious Diseases, Vol l 5, No 4.

Landry, S. & Heilman, H., (2005, May/June), *Future directions in vaccines: The payoffs of basic research*, Health Affairs, *24*(3), 758, 12 pp. Retrieved April 2, 2007, from ProQuest.

Leavitt, M. O. Secretary Department of Health and Human Services, (November 2 2005), *Statement on Pandemic Influenza before U.S. House Committee on Appropriations Subcommittee on Labor, Health and Human Services, and Education*, retrieved on 27 March 2007 from http://www.hhs.gov/asl/testify/t051102a.html

Leitenberg, M., (2002), *Biological Weapons and 'Bioterrorism' in the First Years of the 21st Century*, Center for International and Security Studies, University of Maryland.

Lipton, E., (August 18, 2006), *Project BioShield Stymied*, New York Times, retrieved March 26 2007 from: http://project disaster.com/?p=971.

M2 Presswire, (2006, Aug 29), *Research and Markets: The $1.07 billion Indian Biotech Industry is the Third Largest in the Asia Pacific Region*, Coventry, p. *1.*

M2 Presswire, (2007, Mar 27), *RNCOS: India Leads Asian Biotech Sector*, Coventry, p. 1

Marketline Business Information Center,, Global Biotechnology Industry Profile, retrieved April 14 2007 from: http://dbic.datamonitor.com

MayoClinic On-line, (2006), *Personalized medicine: Tailoring treatment to your genetic profile*, retrieved March19, 2007 via http://www.mayoclinic.com/health/personalized-medicine/CA00078

Mergent, (2006 Dec). *The Asia-Pacific Biotechnology Sectors: A Company and Industry Analysis*, New York.

Miller, J., Engelberg, S., Broad, W., (2001), *Germs: Biological Weapons and America's Secret War*, Simon& Schuster, New York.

Moss, C B., Schmitz, A., Schmitz, T.G., (2006), *First-Generation Genetically Modified Organisms in Agriculture, Journal of Public Affairs, Vol 6.*

Nanooze, retrieved March 29, 2007, from http://www.nanooze.org/english/glossary.html#afm

National Academies of Science, Committee on Defining Science-Based Concerns Associated with Products of Animal Biotechnology, Committee on Agricultural Biotechnology, Health, and the Environment, National Research Council, (2002), *Animal Biotechnology: Science-Based Concerns*, Washington, DC, The National Academies Press, http://www.nap.edu.

National Homeland Security Council, (November 2005), *National Strategy for Pandemic Influenza*, retrieved on 23 March 2007 from http://www.whitehouse.gov/homeland/nspi.pdf

NCGA, (2007, March 26), Understanding the Impact of Higher Corn Prices on Consumer Food Products, retrieved April 3, 2007, from National Corn Growers Association: http://www.ncga.com/ethanol/pdfs/2007/UnderstandingImpactHigherCornPricesConsumerFoodPrices032707.pdf

NEVC, (2007, April), E85 Refueling Stations by State, retrieved April 3, 2007, from National Ethanol Vehicle Coalition: http://www.e85refueling.com/states.php

New York Times, (October 10, 2006), *Pfizer enters vaccine business with the purchase of a British company*, PowderMed, retrieved April 4, 2007, from OCLC FirstSearch

Ochuodho, Z., (2006, April 25), *Africa cannot ignore food biotechnology*, retrieved from http://www.africabiotech.com/news2/Article.php?uid=147.

Offit, P. A., (2005, May/June), *Why are pharmaceutical companies gradually abandoning vaccines?*, Health Affairs, 24(3), 622, 9 pp, retrieved April 2, 2007, from ProQuest.

Osterholm, M. T., (2005), *Preparing for the Next Pandemic*, Foreign Affairs, July/August 2005, retrieved on 27 March 2007 from http://web.ebscohost.com/ehost/detail?vid=2&hid=116&sid=8bddd17a-8c4f=43dc-adeb-7b

Parachini, J., (2001), *Anthrax Attacks, Biological Terrorism and Preventive Responses*, RAND.

Pew Initiative on Food and Biotechnology, (2006), *Options for Future Discussions on Genetically Modified and Cloned Animals*, East Lansing MI, Michigan State University Press, http://www.pewagbiotech.org.

Pilch, R., (2002), *The Bioterrorist Threat in the United States*, in Terrorism and Counterterrorism: Understanding the New Security Environment, McGraw Hill, Iowa.

Plunkett Research, Ltd., *Guide to the Biotech Industry (Customized for Agricultural for Agricultural Biotechnology Market)*; downloaded April 6 2007, http://www/plunkettresearch.com

PriceWaterHouseCoopers, (2007), *Personalized Medicine: The Emerging Pharmacogenomics Revolution*, retrieved March 19, 2007 via http://www.pwc.com/techforecasts/pdfs/ pharmaco-wb-x.pdf

Pringle, E., (August 22, 2006), *Lawmakers Say FDA Better Clean Up Its Act*, Scoop Independent News , retrieved March 26 2007 from : http://www.mvrd.org/NewsArchives.cfm.

Production of Pharmaceuticals, Enzymes and 'Bio' Raw Materials, retrieved March 19 2007 from

Purkitt, H., (2005), *Biowarfare Lessons, Emerging Biosecurity Issues, and Ways to Monitor Dual-Use Biotechnology Trends in the Future*, INSS Occasional Paper 61, retrieved 29 Mar 2007 from http://www.usafa.af.mil/ df/inss/OCP/ocp61.pdf

Rasicot, J., (2007, March 1), *A Look at the Latest in Genes; Students Board Mobile Bioscience Lab to Explore Heredity*, The Washington Post, pp. T.16, retrieved April 26, 2006, from Proquest database.

RFA, (2006), *Industry Statistics*, Retrieved May 17, 2007, from Renewable Fuels Association: http://www.ethanolrfa.org/industry/statistics/

Rosenwald, M., (2006), *The Flu Hunter*, Smithsonian, 36(10). 36-46.

Rotz, L., (2002), *Public Health Assessment of Potential Biological Terrorism Agents*, Emerging Infectious Diseases, Vol 8, No 2.

Salinsky, E., (2004), *Tick-Tock: Preparing for the Next Influenza Pandemic*, National Health Policy Forum.

Scott, A., (2006, Aug 30), *India to Become a Key Pharma Manufacturing Hub*, Chemical Week, 168(29), p. 40.

Standard and Poor's, (2007), Agribusiness Industry Survey, Standard & Poor's, retrieved March 7, 2007, from http://www.netadvantage.standardandpoors.com/NASApp/NetAdvantage/showIndustrySurvey.do?code=agr database.

Staples, B., (2006, May 25), *Why American College Students Hate Science [Letter to The Editor]*, The New York Times, pp. A.25, retrieved April 26, 2006, from Proquest database.

Stevens, C., (2007, February 28), *DOE selects Six Cellulosic Ethanol Plants from up to $385 Million in Federal Funding*, retrieved March 7 2007 from US Department of Energy: http://www.doe.gov/news/4827.htm

Stolar, A., (2006), *Bioterrorism and US Policy Responses: Assessing the Threat of Mass Casualties*, Institute of Peace and Conflict Studies, New Delhi, October 2006.

Thomas, N., (2006), *The Regionalization of Avian Influenza in East Asia*, Asian Survey, XLVI (6).

Tilman, D., Hill, J., (2007, March 25), *Corn Can't Solve Our Problem [Letter to The Editor]*, The Washington Post, retrieved March 25, 2007, from ProQuest database.

Timmerman, L., (2007), Genentech, *Gilead's Struggle to Hire as Biotech Booms*, retrieved 30 March 07 from: http://www.bloomberg.com/apps/news?pid=20601109&sid=aruHm

Tucker, B., (2003), *Biosecurity: Limiting Terrorist Access to Deadly Pathogens*, United States Institute of Peace, Peaceworks No 52.

U.S. Citizenship and Immigration Service (USCIS), (2006, November), *Characteristics of Specialty Occupation Workers (H1-B): Fiscal Year 2005*, retrieved May 15, 2007, from U.S. Department of Homeland Security: http://www.uscis.gov/files/nativedocuments/H1B_FY05_Characteristics.pdf

U.S. Supreme Court, Case No. 04-1350, *KSR International Co. v. Teleflex Inc*, November 28, 2006

Weiss, R., (2006), *Nanotechnology Risks Unknown*, The Washington Post, September 26, 2006, A12.

Williams, K., (2007, January 24), *USDA Announces Plan for $1.6 Billion Investment in Renewable Fuels*, retrieved March 7, 2007, from US Department of Agriculture: http://www.usda.gov/wps/portal/!ut/p/_s.7_0_A/7_0_1RD?printable=true&contenidonly=true.pdf

Yacobucci, B. D., (2007, January 24), *Fuel Ethanol: Background and Public Policy Issues*, Congressional Research Service